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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/444,791	BROCKHAUS ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *233-237,239-243,246-253,255-261 and 274-283* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *233-237,239-243,246-253,255-261,274-283* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/8/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

1. Claims 233-237,239-243,246-253,255-261,274-283 are under consideration. Claims 125,127-130,132,148,149,155-159,213-232, 238,244,245,254,262-273 have been cancelled. The previously pending grounds of rejection as applied to cancelled claims are withdrawn in view of the cancellation of said claims.

2. The objection to the amendment filed 8/30/07 as per enunciated in the previous Office Action, section 2, first paragraph is withdrawn in view of applicants arguments.

3. The amendment filed 8/30/07 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows.

The addition of reference to the deposited vector PTA 7942 has no support in the specification as originally filed. Regarding applicants comments and the Lesslauer declaration, the entire sequence of the deposited sequence needs to be disclosed and applicant should point out where said entire sequence was described in the specification as originally filed. The fact that said construct was made is irrelevant if said construct is not disclosed in the specification as originally filed. There is currently no disclosure in the specification of said construct in the specification as originally filed.

Regarding applicants comments about the specification, page 10, line 34, said sentence states: "DNA sequences which code for insoluble as well as soluble fractions of TNF-binding proteins having an apparent molecular weight of 65 kD/75 kD are also preferred.". This sentence does not disclose the deposited vector PTA 7942. In fact, said sentence does not even refer to a DNA encoding a fusion protein. There is no disclosure in the specification as originally filed of PTA 7942. Regarding the Lesslauer declaration, there is no disclosure in the specification as originally filed of PTA 7942. Applicant is required to cancel the new matter in the reply to this Office Action.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 233-237,239-243,246-252 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of section (b) in claim 233. The specification (page 35) discloses use of a specific unidentified HL60 cDNA library to isolate cDNA encoding the TNFR 75kD. However, the claims encompass use of HL60 cDNA libraries from cells other than those specifically disclosed in the specification (aka the deposited cell line recited the claims wherein said cell is not the specific cell line disclosed in the specification because it is not the specific cell line used by applicant). However, cDNA libraries made from different HL60 cell lines will differ in DNA content due to spontaneous mutation found in HL60 cells (for example, see Monnat, abstract). Thus, the specification discloses a specific library with specific sequences wherein the claims encompass use of HL60 libraries that contain different sequences. In addition, the specification discloses that the search of said cDNA library yielded the CDNA clone of Figure 4. The claims encompass sequences other than that disclosed in Figure 4. Regarding applicants comments, none of the cited references provide evidence that the cell line recited in the claims and the cell line used in the specification are identical.

The previously enunciated rejection as pertaining to section (c) of claim 233 is withdrawn in view of applicants arguments.

There is no support in the specification as originally filed for claims that recite additional subsequences in the sequence of claim 233, as per above, the specification discloses that the search of said HL60 cDNA library yielded the CDNA clone of Figure 4. The claims encompass sequences other than that disclosed in Figure 4.

There is no support in the specification as originally field for recitation in claim 243 of the plasmid PTA 7942 for essentially the same reasons as stated in paragraph 3 of this Office action.

6. Claims 233-237,239-242,274-279 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the . . . claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed inventions.

The only nucleic acid encoding a sequence comprising soluble portions of insoluble TNF binding proteins of a TNF 75 kD receptor disclosed in the specification are those disclosed in the Figures. Claims such as 274 drawn to use of a nucleic acid encoding a TNF receptor wherein the only seqeunce recited in the claim is that of SEQ. ID. No. 10 encompass nucleic acids which encode a vast collection of alleles and mutants of the aformentioned known seqeunce disclosed in the Figures and wherein the identity of said mutants and variants is unknown and unpredictable. Similarly, because the cell line recited in part (b) of claim 233 is not the identical cell line as used by applicants in the specification, said claim encompasses mutants and alleles of the sequences disclosed in the Figures of the instant application. cDNA libraries made from different HL60 cell lines will differ in DNA content due to spontaneous mutation found in HL60 cells (for example, see Monnat, abstract). Thus, the claims would encompass unknown and undescribed mutants and variants of the specific sequences disclosed in the specification wherein the identity of said mutants and variants is unknown and unpredictable. The term “human TNF receptor” (and nucleic acids encoding said molecule) as per used in the specification clearly encompasses mutants, variants and

alleles of said molecule wherein the identity of such molecules is not disclosed in the specification and is unpredictable (see specification, page 2, lines 25-33, page 5, lines 11-25, page 10,lines 3-10, page 11, lines 13-38).

Thus, the written description provided in the specification is not commensurate with the scope of the claimed inventions. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the

sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

Regarding applicants comments, the term "human TNF receptor" (and nucleic acids encoding said molecule) as per used in the specification clearly encompasses mutants, variants and alleles of said molecule wherein the identity of such molecules is not disclosed in the specification and is unpredictable (see specification, page 2, lines 25-33, page 5, lines 11-25, page 10,lines 3-10, page 11, lines 13-38). Thus, the claims encompass a vast unknown array of mutants and variants of the specific sequences disclosed in the specification wherein the identity of said mutants and variants is unknown and unpredictable. The term "human TNF receptor" (and nucleic acids encoding said molecule) as per used in the specification clearly encompasses mutants, variants and alleles of said molecule wherein the identity of such molecules is not disclosed in the specification and is unpredictable (see specification, page 2, lines 25-33, page 5, lines 11-25, page 10,lines 3-10, page 11, lines 13-38). Thus, contrary to applicants assertions, the claims encompass unknown mutants and alleles of TNF receptor other than those disclosed in the prior art. Regarding applicants comments about Capon, said decision does not deal with claims that encompass unknown alleles and mutants of a molecule wherein the identity of said mutants and variants is unknown and unpredictable. Thus, the written description provided in the specification is not commensurate with the scope of the claimed inventions. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240.

7. Regarding priority for the claimed inventions and the application of prior art, the claimed nucleic acids encoding fusion proteins are not disclosed in the Swiss priority documents. SEQ ID. NO: 27 is not disclosed in said applications. The vectors recited in the claims are also not disclosed in said applications. Also, the correct sequence for the DNA encoding the TNF 75 kD receptor (as per page 35, last paragraph of the specification) is not disclosed in said applications.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 233-237,239-243,246-253,255-261,274-283 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (US Patent 5,395,760) in view of Capon et al. (US Patent 5428130).

Smith et al. teach DNA encoding an insoluble (eg. membrane bound) 75 kD TNF receptor that has the amino acid sequence of SEQ. ID. NO:27 (see Figure 2). Smith et al. teach the soluble extracellular portion of said molecule (see column 4). Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor (see column 10, last paragraph). Smith et al. do not teach a nucleic acid encoding an Ig/soluble portion of a 75kD TNF receptor wherein the IG portion lacks the first domain of the constant region. This rejection addresses the TNF-R nucleic acid sequence of claims 233/243 as encompassing SEQ. ID. NO:27. Capon et al. teach DNA encoding Ig/ligand binding fusion proteins (see column 5). Capon et al. teach that the Ig/ligand binding fusion protein can contain the soluble portion of a cell surface receptor (eg. the receptor minus the transmembrane and cytoplasmic domains, see column 8, first complete paragraph). Capon et al. teach that the DNA encoding the Ig portion of the fusion protein can contain at least the hinge, CH2 and CH3 domains of the constant region of an Ig heavy chain or the Fc portion of the heavy chain (see column 10, second paragraph). Capon et al. teach vectors /host

cells containing said DNA and use of said cells to produce fusion protein (see column 26-30). Capon teach the use of IgG-1 constant region in said fusion proteins (see claim 3). Capon et al. teach that the ligand binding portion of the Ig/ligand binding fusion protein can be derived from a wide variety of different known cell surface receptors (see column 7, third paragraph from bottom). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Smith et al. teach the nucleic acid sequence encoding an insoluble (eg. membrane bound) 75kD TNF receptor and DNA encoding bivalent Ig fusion proteins containing said molecule while Capon et al. teach DNA encoding soluble Ig/ligand binding fusion proteins wherein the DNA encoding the Ig portion of the fusion protein can contain at least the hinge, CH2 and CH3 domains of the constant region of an Ig heavy chain and wherein the ligand binding protein is a soluble portion derived from a cell surface receptor. One of ordinary skill in the art would have been motivated to do the aforementioned because Capon et al. teach that the ligand binding portion of the Ig/ligand binding fusion protein can be derived from a wide variety of different known cell surface receptors (see column 7, third paragraph from bottom) and that said fusion proteins have a variety of a uses (see column 4). The IgG1 constant region fragment encoding nucleic acids of pCD4Hgamma1 appear to be the art known nucleic acids encoding the portion of the human IgG1 constant region as per disclosed in Capon et al. In addition, Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor.

Regarding applicants comments about unexpected results, the claimed inventions are drawn to nucleic acids, not proteins. There is no evidence of record regarding unexpected results and the claimed invention (aka nucleic acids). However, as per the interview of 8/4/2010, the putative "unexpected results" regarding the protein will be addressed. The MPEP section 716.02(e) states:

716.02(e) [R-2] Comparison With Closest Prior Art

An affidavit or declaration under 37 CFR 1.132 must compare the claimed subject matter with the closest prior art to be effective to rebut a prima facie case of obviousness. In re Burckel, 592 F.2d 1175, 201 USPQ 67 (CCPA 1979). "A comparison of the claimed invention with the disclosure of each cited reference to determine the number of claim limitations in common with each reference, bearing in mind the relative

importance of particular limitations, will usually yield the closest single prior art reference." In re Merchant, 575 F.2d 865, 868, 197 USPQ 785, 787 (CCPA 1978) (emphasis in original). Where the comparison is not identical with the reference disclosure, deviations therefrom should be explained, In re Finley, 174 F.2d 130, 81 USPQ 383 (CCPA 1949), and if not explained should be noted and evaluated, and if significant, explanation should be required. In re Armstrong, 280 F.2d 132, 126 USPQ 281 (CCPA 1960) (deviations from example were inconsequential).

In the instant rejection, the closest prior art is the nucleic acid encoding an IgG/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor as per taught by Smith et al. However, none of the cited alleged unexpected results regarding the claimed invention compare the instant invention to the closest prior art. The studies using soluble TNF receptor do not compare the claimed invention to the closest prior art. CD4 soluble fusion proteins do not even contain TNF receptor and do not constitute the "closest prior art". CD4 binds a molecule that has no relation to TNF or the TNF receptor and wherein the ligand for said molecule is not even a soluble protein (aka it is a cell surface bound molecule). Regarding applicant comments about anti TNF antibodies, said molecules are structurally and functionally distinct from the claimed invention. For example, said molecules do not contain a "TNF receptor" as per recited in the claimed invention. Furthermore, the binding of said antibodies is totally mediated by a unique combination of CDR/FR regions that are found in the antibody variable region wherein said CDR/FR regions are not found in the claimed invention. As per above, the closest prior art is the nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor as per taught by Smith et al.

Regarding applicants comments, Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor (see column 10, last paragraph). Smith et al. do not teach a nucleic acid encoding an Ig/soluble portion of a 75kD TNF receptor wherein the IG portion lacks the first domain of the constant region. Capon et al. teach DNA encoding Ig/ligand binding fusion proteins (see column 5). Capon et al. teach that the Ig/ligand binding fusion protein can contain the soluble portion of a cell surface receptor (eg. the receptor minus the transmembrane and cytoplasmic domains, see column 8, first complete paragraph).

Capon et al. teach that the DNA encoding the Ig portion of the fusion protein can contain at least the hinge, CH2 and CH3 domains of the constant region of an Ig heavy chain or the Fc portion of the heavy chain (see column 10, second paragraph). In fact, Capon et al., column 10, second paragraph teach that:

> *Typically, such fusions retain at least functionally active hinge, CH2 and CH3 domains of the constant region of an immunoglobulin heavy chain. Fusions are also made to the C-terminus of the Fc portion of a constant domain, or immediately N-terminal to the CH1 of the heavy chain or the corresponding region of the light chain. This ordinarily is accomplished by constructing the appropriate DNA sequence and expressing it in recombinant cell culture.*

Thus, Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor (see column 10, last paragraph) whilst Capon et al. teach that such molecules can be made wherein the CH1 domain is omitted. Also, it is noted that Smith et al. teach that the fusion protein is bivalent (aka it contains only two copies of the TNF R molecule, see column 10, last paragraph) wherein said molecule is produced from a single heavy constant and light chain constant region. It is further noted that the references related to etanercept indicate that said molecule has a IgG1 constant region. Claims that do not recite an IgG1 constant region encompass other IgG constant regions wherein the results related to etanerecept are not germane to constant regions other than IgG1. It is also unclear as what the amino acid sequence of etanercept is and whether said seqeunce is of the scope of the claimed invention. Regarding applicants comments about aggregation and Larsson et al., the claimed molecules encode TNF receptor wherein the Larsson et al. reference does not address TNF receptor. In fact, said reference is not even drawn to the interaction of protein receptor/protein ligand. The reference involves interaction of an enzyme with a nonprotein ligand that is not germane to the claimed invention.

10. The rejection of claims 224-232,253-261,266,267,272,273 under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (Science, 1990) in view of Capon et al. (US Patent 5428130) as per the previous Office is withdrawn in view of the cancellation of claims that have been cancelled and because the Smith et al. (Science, 1990)

reference lacks the specific teaching of a TNF R/IgG fusion protein as per found in the Smith et al. (US Patent 5,395,760) as per cited above.

11. Claims 233-237,239-243,246-253,255-261,274-283 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dembic et al. (Cytokine, 1990) in view of Smith et al. (US Patent 5,395,760) Capon et al. (US Patent 5428130).

Dembic et al. teach DNA encoding an insoluble (eg. membrane bound) 75 kD TNF receptor that is derived from HL60 cells and that encodes the various peptide fragments recited in the claims (see page 231, second column). Dembic et al. teach the extracellular portion of said molecule (see abstract). The extracellular portion of the membrane bound molecule would be a soluble portion of said molecule. Dembic et al. do not teach a nucleic acid encoding an Ig/soluble portion of a 75kD TNF receptor. Smith et al. teach DNA encoding an insoluble (eg. membrane bound) 75 kD TNF receptor that has the amino acid seqeunce of SEQ. ID. NO:27 (see Figure 2). Smith et al. teach the soluble extracellular portion of said molecule (see column 4). Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor (see column 10, last paragraph). Smith et al. do not teach a nucleic acid encoding an Ig/soluble portion of a 75kD TNF receptor wherein the IG portion lacks the first domain of the constant region. This rejection addresses the seqeunce of claim 243 as encompassing SEQ. ID No 27 or the HL-60 relate seqeunce of claim 233. Capon et al. teach DNA encoding Ig/ligand binding fusion proteins (see column 5). Capon et al. teach that the Ig/ligand binding fusion protein can contain the soluble portion of a cell surface receptor (eg. the receptor minus the transmembrane and cytoplasmic domains, see column 8, first complete paragraph). Capon et al. teach that the DNA encoding the Ig portion of the fusion protein can contain at least the hinge, CH2 and CH3 domains of the constant region of an Ig heavy chain or the Fc portion of the heavy chain (see column 10, second paragraph). Capon et al. teach vectors /host cells containing said DNA and use of said cells to produce fusion protein (see column 26-30). Capon teach the use of IgG-1 constant region in said fusion proteins (see claim 3). Capon et al. teach that the ligand binding portion of the Ig/ligand binding fusion protein can be derived from a wide variety of different known cell surface receptors (see column 7, third paragraph from bottom). It would have been

prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Dembic et al. teach DNA encoding an insoluble (eg. membrane bound) 75 kD TNF receptor that is derived from HL60 cells, Smith et al. teach the nucleic acid sequence encoding an insoluble (eg. membrane bound) 75kD TNF receptor and DNA encoding bivalent Ig fusion proteins containing said molecule while Capon et al. teach DNA encoding soluble Ig/ligand binding fusion proteins wherein the DNA encoding the Ig portion of the fusion protein can contain at least the hinge, CH2 and CH3 domains of the constant region of an Ig heavy chain and wherein the ligand binding protein is a soluble portion derived from a cell surface receptor. One of ordinary skill in the art would have been motivated to do the aforementioned because Capon et al. teach that the ligand binding portion of the Ig/ligand binding fusion protein can be derived from a wide variety of different known cell surface receptors (see column 7, third paragraph from bottom) and that said fusion proteins have a variety of a uses (see column 4). The IgG1 constant region fragment encoding nucleic acids of pCD4Hgamma1 appear to be the art known nucleic acids encoding the portion of the human IgG1 constant region as per disclosed in Capon et al. In addition, Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor.

Applicants arguments are as per addressed above.

12. Claims 233-237,239-243,246-253,255-261,274-283 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (US Patent 5,395,760) in view of Hohmann et al. (J. Biol. Chem., 1989) and Capon et al. (US Patent 5428130).
Smith et al. teach DNA encoding an insoluble (eg. membrane bound) 75 kD TNF receptor that has the amino acid seqeunce of SEQ. ID. NO:27 (see Figure 2). Smith et al. teach the soluble extracellular portion of said molecule (see column 4). Smith et al. teach DNA encoding an Ig fusion molecule. Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor (see column 10, last paragraph). Smith et al. do not teach a nucleic acid encoding an Ig/soluble portion of a 75kD TNF receptor wherein the Ig portion lacks the first domain of the constant region and wherein the DNA encodes the 75 kD TNF receptor in HL-60 cells. This rejection addresses the sequence of claim 233 as

encompassing other than SEQ. ID. No. 27. Smith et al. teach that nucleic acids encoding the 75 kD TNF receptor can isolated from mammalian cells that express said receptor and method for isolating said DNA (see columns 5-6). Hohmann et al. teach that HL-60 cells express the TNF 75 kD receptor (see page 14929). Whilst the identity of the sequence encoding the TNF receptor 75 kD in the construct of claim 233 is unclear, since it was apparently derived from HL60 cells it will be considered as encoding the same HL60 sequence as found in said cells. Capon et al. teach DNA encoding Ig/ligand binding fusion proteins (see column 5). Capon et al. teach that the Ig/ligand binding fusion protein can contain the soluble portion of a cell surface receptor (eg. the receptor minus the transmembrane and cytoplasmic domains, see column 8, first complete paragraph). Capon et al. teach that the DNA encoding the Ig portion of the fusion protein can contain at least the hinge, CH2 and CH3 domains of the constant region of an Ig heavy chain or the Fc portion of the heavy chain (see column 10, second paragraph). Capon et al. teach vectors /host cells containing said DNA and use of said cells to produce fusion protein (see column 26-30). Capon teach the use of IgG-1 constant region in said fusion proteins (see claim 3). Capon et al. teach that the ligand binding portion of the Ig/ligand binding fusion protein can be derived from a wide variety of different known cell surface receptors (see column 7, third paragraph from bottom). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor (see column 10, last paragraph) and Smith et al. teach that nucleic acids encoding the 75 kD TNF receptor can isolated from mammalian cells that express said receptor and method for isolating said DNA whilst Hohmann et al. teach that HL-60 cells express the TNF 75 kD receptor while Capon et al. teach DNA encoding soluble Ig/ligand binding fusion proteins wherein the DNA encoding the Ig portion of the fusion protein can contain at least the hinge, CH2 and CH3 domains of the constant region of an Ig heavy chain and wherein the ligand binding protein is a soluble portion derived from a cell surface receptor. One of ordinary skill in the art would have been motivated to do the aforementioned because Capon et al. teach that the ligand binding portion of the Ig/ligand binding fusion protein can be derived from a wide variety of different known cell surface receptors (see column 7, third

paragraph from bottom) and that said fusion proteins have a variety of a uses (see column 4) and Smith et al. teach that nucleic acids encoding the 75 kD TNF receptor can isolated from mammalian cells that express said receptor and method for isolating whilst Hohmann et al. teach that HL-60 cells express the TNF 75 kD receptor. The IgG1 constant region fragment encoding nucleic acids of pCD4Hgamma1 appear to be the art known nucleic acids encoding the portion of the human IgG1 constant region as per disclosed in Capon et al. In addition, Smith et al. teach a nucleic acid encoding an IgG1/soluble portion of a 75kD TNF receptor wherein the fusion protein is bivalent for TNF receptor.

Applicants arguments are as per addressed above.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is (571)272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/
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Art Unit 1644